

***Remarks***

Reconsideration of this Application is respectfully requested.

By this amendment, the specification as originally filed is sought to be amended by the addition of FIG 8A-8C to the drawings section. Likewise, a new paragraph providing a brief description of new FIG 8A-8C is sought to be entered after paragraph 0037, on pages 14-15 of the specification as originally filed. Support for these amendments can be found in the specification as originally filed on page 25, paragraph 0071, wherein U.S. Patent No. 5,668,005 (the '005 patent) is incorporated by reference. The '005 patent discloses the amino acid sequence represented by SEQ ID NO: 6 in FIG. 6A-6B on sheets 6-8 of the drawings section of the '005 patent, and provides support for the description of newly added FIG 8A-8C at column 9, lines 4-7. Since the '005 patent was incorporated by reference in its entirety into the present specification as originally filed, the foregoing amendments to the drawings and specification do not add new matter to the specification. *See* MPEP § 608.01(p).

Claims 91 and 103 have been amended to specifically recite a wild type polymerase domain amino acid sequence within SEQ ID NO: 6, and that amino acid number 1 of SEQ ID NO: 6 is the threonine following the initial methionine. Support for the amendment can be found in the specification as originally filed on page 25, paragraph 0071, wherein U.S. Patent No. 5,668,005 (the '005 patent) is incorporated by reference. The '005 patent discloses the amino acid sequence represented by SEQ ID NO: 6 in FIG. 6A-6B on sheets 6-8 of the drawings section of the '005 patent. Support for recitation that amino acid number 1 of SEQ ID NO: 6 is the threonine following the

initial methionine may be found in the specification at [0161] which states that wild type MMLV does not start with a methionine.

Upon entry of the foregoing amendments, claims 91-101, 103, 107, 110-112, 114-117, 119 and 120 are pending in the application, with claims 91 and 103 being the independent claim. Claims 91, 103, 112 and 117 have been amended. These amendments introduce no new matter, and their entry is respectfully requested.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

**Rejections Under 35 U.S.C. § 112, first paragraph (written description)**

Claims 91-101, 103, 107 and 110-120 were rejected for containing subject matter that was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Office Action, pages 3-10. The main assertions raised in this section are that: 1) the claim permits any sequence that has reverse transcriptase activity; 2) the reverse transcriptase is defined solely by function; and 3) the genus includes variants for which no written description is provided in the specification.

In the presently amended claims, the recited mutant MMLV reverse transcriptase comprises a polymerase domain having particular substitutions in the amino acid sequence of the wild type MMLV polymerase domain within SEQ ID NO: 6. Thus, the MMLV reverse transcriptases of the presently claimed invention share at least the common element of having a polymerase domain within SEQ ID NO: 6. In addition to showing possession of the claimed invention at the time of filing, this structural

recitation positively identifies sequences that result in enhanced fidelity. Thus, the current claims encompass a particular genus of mutant reverse transcriptases, which have the recited structural feature and do not encompass any conceivable sequence that has reverse transcriptase activity since the reverse transcriptase comprises a polymerase domain within the recited SEQ ID NO. In addition, the claimed reverse transcriptase is defined by structure, and not solely by function. Clearly, one of ordinary skill in the art would have reasonably concluded that the inventors had possession of the claimed substitution mutants when the application was filed. Therefore, the claimed genus was adequately described.

In view of the foregoing remarks, Applicants respectfully submit that the specification fully describes the claimed invention. Thus, reconsideration and withdrawal of the rejection under 35 U.S.C. 112, first paragraph, are respectfully requested.

**Rejection Under 35 U.S.C. §112, first paragraph (new matter)**

Claims 112, 113, 117 and 118 were rejected as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the recitation of “Asp544” was considered to be new matter. Claims 113 and 118 have been canceled. Claims 112 and 117 as amended no longer recite “Asp544”. Thus, this rejection is now moot. Reconsideration and withdrawal of the rejection under 35 U.S.C. 112, first paragraph, are therefore respectfully requested.

**Claim Interpretation**

The Office Action states that "these claims actually read on any active reverse transcriptase enzyme whatsoever, since the amino acids surrounding the particular residues are not restricted to belong to any particular sequence, and, therefore, they do not possess any other structural constraints." Office Action at page 11. The interpretation given to claims during examination must be of a breadth consistent with the interpretation given by an artisan of ordinary skill. *In re Cortright*, 165 F.3d 1353, 1359 (Fed. Cir. 1999); MPEP 2111 at p. 2100-47 (8<sup>th</sup> ed., Rev. 1, Feb. 2003). Moreover, claim terms need only be as precise as the art. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).

As amended, the claims recite mutant MMLV reverse transcriptases that comprise a polymerase domain and particular amino acid substitutions in the amino acid sequence of the wild type MMLV polymerase domain within SEQ ID NO: 6. This clearly provides structural and sequence support for the claimed subject matter. Thus, the assertion that the claims read on any reverse transcriptase whatsoever is clearly incorrect and cannot be used as a basis for rejections under 35 U.S.C § 102(b) and 35 U.S.C § 103 on pages 12-15 of the Office Action.

**Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 111-115 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. On page 12, line 5 of the Office Action, it was stated that the term "said reverse transcriptase has substantially reduced RNase activity" was indefinite since it was not clear how this activity was determined.

The specification at page 25, lines 3-8, states that “the RNase activity of any enzyme may be determined by a variety of assays, such as those described, for example, in U.S. Patent Nos. 5,244,797; 5,405,776; 5,668,005 and 6,063,608; in Kotewicz, M.L., et al., Nucl. Acids Res. 16:265, (1988); and in Gerard, G.F. et al., FOCUS 14(5):91 (1992), the disclosures of which are fully incorporated herein by reference.” Since determination of RNase H activity is well known and described in U.S. Patents which are incorporated by reference, claims 111-115 are not indefinite.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

**Rejection Under 35 U.S.C. § 102(b)-Kotewicz et al.**

Claims 91, 92, 94, 96, 98, 100, 107, 111 and 116 were rejected under 35 U.S.C. § 102(b) as being anticipated by Kotewicz et al. (U. S. Patent No. 5,244,797). Applicants respectfully traverse this rejection.

Claims 91 and 103 as amended recites particular substitutions in the amino acid sequence of the wild type MMLV polymerase domain within SEQ ID NO: 6 in which the first amino acid of the reverse transcriptase is the threonine following the initial methionine. The present specification states that wild type MMLV does not start with a methionine. Specification at [0161]. Thus, the methionine listed in the MMLV sequence of Kotewicz et al. is not present in the claimed sequence. Accordingly, the numbering of the amino acid positions of Kotewicz et al. should reduced by one, such that the first methionine is removed, and the threonine at position 2 becomes the first amino acid in the MMLV sequence. Consequently, the alleged Glu64, Leu116, Asn152, Ala190, Glu197 and Val309 in Kotewicz et al. are actually Glu63, Leu115, Asn151,

Ala189, Glu196 and Val308. Thus, the amino acids at positions 64, 116, 152, 190, 197 and 309 of the sequence in Kotewicz *et al.* are Tyr64, Arg116, Lys152, Gln190, Thr197, and Phe309 respectively. Since claim 91 recites at least one mutation at an amino acid position selected from the group consisting of Tyr64, Arg116, Lys152, Gln190, Thr197, and Phe309, and Kotewicz *et al.* do not disclose any mutations at these positions, the claims are not anticipated.

Thus, Kotewicz *et al.* do not teach or suggest the amino acid substitutions recited in the pending claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102 (b).

**Rejection Under 35 U.S.C. § 102(b)-Hizi *et al.***

Claims 91, 92, 94, 96, 98, 100, 107, 111, 112, 116 and 117 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hizi *et al.* (*Virology* **175**:575-580, 1990) as evidenced by Schatz *et al.* (*FEBS Letters* **257**:311-314, 1989). Applicants respectfully traverse the rejection.

Claim 91 as amended recites a mutant MMLV reverse transcriptase comprising particular substitutions in the amino acid sequence of the wild type MMLV polymerase domain within SEQ ID NO: 6. Hizi *et al.* teach a MMLV RT-HIV-1 RT fusion protein, not a mutant MMLV reverse transcriptase as presently claimed. Thus, the claims are not anticipated by Hizi *et al.* Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

**Rejection Under 35 U.S.C. § 102(b)-Georgiadis et al.**

Claims 91, 92, 94, 96, 98 and 100 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Georgiadis *et al.* (*Structure* 3:879-892, 1995). Applicants respectfully traverse the rejection. Claim 91 as amended recites a mutant MMLV reverse transcriptase comprising particular substitutions in the amino acid sequence of the wild type MMLV polymerase domain within SEQ ID NO: 6. Georgiadis et al. teach an HIV-1 RT fusion protein, not a mutant MMLV reverse transcriptase as presently claimed. Thus, the claims are not anticipated by Georgiadis et al. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

**Obviousness-Type Double Patenting Rejection**

Claims 91, 92, 96 and 107 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 3, 5 and 6 of copending Application No. 10/661,819. It was alleged that claims 2, 3, 5 and 6 are species of claims 91, 92, 96 and 107.

Claims 91, 100, 107, 110, 111, 112, 114, 115, 117, 119 and 120 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19, 20, 22, 23, 25, 26, 28 and 29 of copending Application No. 09/845,157. It was alleged that claims 19, 20, 22, 23, 25, 26, 28 and 29 of copending Application No. 09/845,157 are species of claims 91, 100, 107, 110, 111, 112, 114, 115, 117, 119 and 120 of the instant application.

Applicants respectfully request that these rejections be held in abeyance until the subject matter in one of these applications has been deemed allowable.

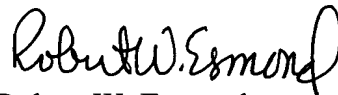
***Conclusion***

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply and allowance of all pending claims, are respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Robert W. Esmond  
Attorney for Applicants  
Registration No. 32,893

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1100 New York Avenue, N.W.  
Washington, D.C. 20005-393418  
(202) 371-2600